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ORIGINAL ARTICLE

Usage of B-type natriuretic peptide for prediction of weaning outcome by spontaneous breathing trial



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KEYWORDS

B-type natriuretic peptide;
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Abstract *Background:* Prediction of weaning success remains a major clinical challenge. Cardiovascular dysfunction could be a major underlying mechanism of weaning failure. Recent data suggest that BNP; a marker for cardiovascular dysfunction, may predict the outcome of weaning from assisted mechanical ventilation. BNP variations during spontaneous breathing trial may be of predictive value concerning the outcome of weaning process.

Objective: To evaluate the role of BNP levels measured during a 2 h. SBT as a predictive value for weaning outcome.

Method: A prospective observational study included forty patients on mechanical ventilation who underwent an SBT. Echocardiography was done 2 h, before SBT and sampling of BNP was performed immediately before and at the end of SBT to determine the predictive value of BNP.

Results: Patients were divided according to the result of the 2-h SBT into 3 groups: SBT failure [8 pts.], extubation success [25 pts.] and extubation failure [7 pts.]. The BNP level was significantly higher in SBT failure and extubation failure groups after SBT than before SBT while it was significantly lower in the extubation success group after SBT than before SBT with a *p*-value of 0.004. It was found that both extubation and SBT failure groups had significantly larger percent increase in BNP level unlike the extubation success group who had significantly percent decrease in the BNP level with a *p*-value < 0.001. The area under the ROC curve was 0.96. A change of BNP level < 20% from baseline had the best combination of sensitivity [85.71%], specificity [90.91%], positive [96.77%] and negative [66.67%] predictive values and diagnostic accuracy [90%] in predicting extubation failure.

Conclusion: BNP level variation during SBT may improve the predictive value of the trial on weaning outcome.

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Introduction

Liberating a patient from mechanical ventilation remains a significant challenge for clinicians [1]. Complications of invasive mechanical ventilation increase with the duration of ventilator dependence [2]. Patients should therefore be weaned from mechanical ventilation as quickly as possible. However, both delayed and premature weaning may be harmful [2,3]. The 2 h. spontaneous breathing trial (SBT) is currently the most accurate index for predicting weaning success, but the extubation failure rate is still high (15–20%) in patients who have passed SBTs [1]. The causes and pathophysiology underlying weaning failure is complex [4]. The relative weight of the different factors involved is not completely understood. Cardiac function and, more importantly, volume status may play a key role in this setting [5]. In critically ill patients, however, it is difficult to detect cardiovascular dysfunction in the dynamic process of weaning using the traditional methods such as echocardiography, cardiac scintiscan and pulmonary artery catheterization that are either operator-dependent, lacking sensitivity, not available at the bedside, or invasive [6]. B-type natriuretic peptide (BNP) is a 32-amino acid protein released from the cardiac ventricles in response to myocardial stretch [7]. BNP is the most powerful hormonal predictor of left-ventricular dysfunction, and its plasma level has been correlated to left-ventricular filling pressures [8]. Plasma BNP levels are elevated in acute congestive heart failure [9] and right ventricular dysfunction [10].

Aim of the work

To determine whether BNP levels measured during a 2 h. SBT could improve the predictive value for weaning outcome.

Patients and methods

Patients

The study protocol was approved by the local ethics committee. We randomly and prospectively enrolled forty mechanically ventilated patients admitted consecutively to the critical care department; faculty of medicine-Cairo university hospital; from May 2010 till June 2011. Informed consent was given by a close relative (first degree).

Inclusion criteria

Patients being considered for liberation from mechanical ventilation support for the first time were enrolled in our study. To be enrolled in our study; patient needed to show improvement or resolution of the underlying causes of Respiratory failure indicated by $\text{PaO}_2 \geq 60$ mm Hg at $\text{FiO}_2 \leq 40\%$ and a $\text{PEEP} \leq 5$ cm H_2O , $\text{GCS} \geq 13$, temperature $< 38^\circ\text{C}$ and hemodynamically stable with a mean blood pressure ≥ 65 mm Hg and without the use of vasoactive agents for at least 24 h.

Exclusion criteria

Patients with left ventricular failure, right ventricular failure, pulmonary hypertension, aortic valve disease, atrial

fibrillation, renal impairment, hyperthyroidism, cerebrovascular strokes, anemia, liver cirrhosis, tracheostomy and obesity were excluded from the study as these conditions may be associated with increased BNP levels.

All included patients were subjected to the following:

1. *Full Clinical Evaluation:* Including demographic data, full medical history of present illness, pre-existing comorbidity and full clinical examination including baseline hemodynamics.
2. *Laboratory Investigations:*
 - Routine labs: CBC (complete blood count): Hemoglobin, Hematocrit, White blood cells and platelet count, Coagulation profile: PT (prothrombin time), PC (prothrombin concentration), INR and PTT (partial thromboplastin time), Liver function tests: ALT (Alanine aminotransferase), AST (Aspartate aminotransferase), BIL (bilirubin) total and direct and albumin, Kidney Function Tests: Na, K, Creatinine and Urea, Thyroid profile (freeT_3 , freeT_4 , and TSH) and Serum electrolytes (Sodium, Potassium & Calcium). These routine Labs were withdrawn on day 1 of the study.
 - Serial Arterial blood gases.
 - BNP measurement: This was done by the use of BNP-32 (human) EIA kit provided by Phoenix pharmaceuticals, INC. This kit is designed to detect a specific peptide and its related peptides based on the principle of competitive enzyme immunoassay.

Blood sampling

Blood samples were collected from patients before and after SBT as follows: 7 ml of venous blood was drawn into tubes containing EDTA for anticoagulation & aprotinin (protease inhibitor), each tube was gently rocked several times immediately after collection of blood to prevent blood clotting and inhibit the activity of proteases, then centrifuged for 15 min at 4°C and plasma was collected in eppendorf tubes and kept at -70°C till analysis within 4 h using a fully automated micro particle enzyme immunoassay by the use of the BNP-32 (human) EIA kit provided by phoenix pharmaceutical INC.

Principle of the assay

The immunoplate in the kit is pre-coated with secondary antibody and the non-specific binding sites are blocked. The secondary antibody can bind to the Fc fragment of the primary antibody (peptide antibody) whose Fab fragment will be competitively bound by both biotinylated peptide and peptide standard or targeted peptide in samples. The biotinylated peptide interacts with streptavidine-horseradish peroxidase (SA-HRP) which catalyzes the substrate solution. The intensity of the yellow is directly proportional to the amount of biotinylated peptide-SA-HRP complex but inversely proportional to the amount of the peptide in standard solutions or samples. This is due to the competitive binding of the biotinylated peptide with the standard peptide or samples to the peptide antibody (primary antibody). A standard curve of known concentration was established accordingly. The unknown

concentration in samples can be determined by extrapolation to this standard curve.

Assay procedure

The kit was stored at 4 °C and all kit components were allowed to return to room temperature (20–23 °C) before use (25–45min). The assay buffer concentrate was diluted with 950 ml of distilled water to dilute or reconstitute all other reagents in this kit and samples. Centrifugation of the standard peptide was done with 1 ml of the diluted assay buffer. Rehydration of the primary antibody was done with 5 ml of diluted assay buffer. Rehydration of biotinylated peptide was done with 5 ml of diluted buffer. Centrifugation of the standard peptide was done with 1 ml of the diluted assay buffer. Centrifugation & rehydration of the positive control were done with 200 ml of diluted assay buffer. Two wells were left empty as a blank. 50 µl of each of the prepared standards was dispensed into designated wells. 25 µl of rehydrated primary antibody was added into each well except the blank well. 25 µl of rehydrated biotinylated peptide was added into each well except the blank well. The immunoplate was sealed with acetate plate sealer (APS) and incubated for 2 h at room temperature. The SA-HRP vial was centrifuged for 5 s and 12 ml of SAHRP was added to 12 ml of diluted assay buffer to make SA-HRP solution. 100 µl of SA-HRP solution was added into each well. 100 µl of TMB substrate solution was added into each well. 100 µl of 2 N HCl was added into each well to stop the reaction. The wells were left till their color changed from blue to yellow before reading. The immunoplate was loaded onto a Micro-titer Plate Reader. Absorbance was read at 450 nm.

Calculation of results

The standard curve was plotted on a semi-log graph paper. It was constructed by plotting the known concentrations of standard peptide on the log scale and its corresponding O.D. reading on the linear scale. The standard curve shows an inverse relationship between peptide concentrations and the corresponding absorbance. As the standard concentration increases, the yellow color decreases, thereby reducing the O.D. absorbance.

1. *Standard 12 leads ECG:* to detect ischemia and to exclude atrial fibrillation.
2. *Imaging studies:* Echocardiography; was done for all patients 2 h, before SBT to assess Left ventricular dimensions & contractility. The left ventricular ejection fraction (LVEF) was calculated by the biplane modified Simpson's method from the apical 4-chamber view by an echo cardiographer who was blind to patient weaning outcome and BNP levels.
3. *Protocol of the spontaneous breathing trial:* When mechanically ventilated patients were placed on low pressure support (6–10 cm H₂O) for at least 2 h, mechanical ventilation was stopped and the patient was allowed to breathe spontaneously through at T-tube (SBT) with the same Fio₂.

On the basis of the clinical findings, patients were subdivided according to the outcome of the 2-h SBT into 3 groups: Group A: SBT failure, Group B: extubation success and Group C: extubation failure.

Patients were considered to have failed SBT if they developed any of the following during the 2-h SBT [37]:

1. Respiratory frequency ≥ 35 breaths per minute.
2. Arterial oxygen saturation $< 90\%$.
3. Heart rate ≥ 140 beats per minute or a sustained increase or decrease in heart rate $> 20\%$.
4. Systolic blood pressure > 180 mm Hg or < 90 mm Hg.
5. Thoraco-abdominal dys-synchrony, agitation, diaphoresis, or anxiety.

Patients who had none of these features at the end of the SBT were subsequently extubated. After extubation, the patients were closely monitored for 48 h. Patients were re-intubated if they developed one of the following signs:

1. Hypoxemia: SaO₂ $< 90\%$ or PaO₂ < 60 mmHg at FIO₂ $> 50\%$.
2. Respiratory acidosis: PH < 7.30 with PCO₂ > 50 mm Hg.
3. Clinical signs of respiratory distress including at least one of the following: Thoraco-abdominal desynchrony, retraction of intercostal spaces, use of the accessory muscles, agitation, increasing of the respiratory rate > 35 bpm and sustained increase in heart rate $> 20\%$.

Statistics

Data were statistically described in terms of range, mean, standard deviation (\pm SD), median, frequencies (number of cases) and percentages when appropriate. Comparison of quantitative variables between the study groups was done using Mann Whitney *U* test for independent samples. For comparing categorical data, Chi square (χ^2) test was performed. Exact test was used instead when the expected frequency is less than 5. Receiver operator characteristic (ROC) analysis was used to determine the optimum cut off value for the studied diagnostic markers. Correlation between various variables was done using Spearman rank correlation equation for non-normal variables. A probability value (*p* value) less than 0.05 was considered statistically significant. Statistical calculations were done using computer program Microsoft Excel 2003 (Microsoft Corporation, NY, USA) and SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) version 15 for Microsoft Windows.

Results

1. Demographic and baseline clinical characteristics of the patient population on admission (Table 1).
2. Classification of patients according to SBT trial (Table 2).
3. Clinical characteristics of different study groups (Table 3).
4. BNP level before and after SBT in different study groups: The BNP level was significantly higher in SBT failure and extubation failure groups after SBT than before SBT while it was significantly lower in the extubation success group after SBT than before SBT with a *p*-value of 0.004 (Table 4).
5. The mean percent change in plasma BNP level during 2-h. SBT: The mean percent change in BNP level during the 2-h. SBT in the extubation success group showed significantly

Table 1 Demographic and baseline clinical characteristics of the patients on admission.

Characteristics	Patients groups
Number of patients	40
Age; mean \pm SD in years (range)	48.80 \pm 10.19(28–69)
Male:Female sex (ratio & percentage)	26:14 (65:35%)
<i>Causes of ARF (number & percentage)</i>	
ARDS	12 (30%)
COPD	4 (15%)
Pneumonia	12 (30%)
Sepsis	12 (30%)
<i>Comorbidity (number & percentage)</i>	
Hypertension	28 (70%)
Diabetes Mellitus	19 (47%)
Ischemic Heart Disease	8 (20%)
<i>Risk factor (number & percentage)</i>	
Smoking	24 (60%)

Table 2 Classification of patients according to SBT trial.

Groups	SBT failure	SBT success	
		Extubation failure	Extubation Success
Number	8	7	25
Percentage (%)	20%	17.5%	62.5%

percent decrease in the BNP level [24.987%] than in the SBT failure [36.723%] and extubation failure [34.226%] groups who showed significantly percent increase with a p -value < 0.001 (Table 5).

6. Correlation between BNP level and LVEF% in different study groups: No significant correlation was found between BNP before SBT and LVEF% (Table 6).

7. ABG before and after SBT in different study groups: There was a significant decrease in PO₂ level and oxygen saturation in both SBT failure and extubation failure group after the SBT trial while there was no significant change in the ABG parameters in the Extubation success group (Table 7).
8. Predictive value of the percent change in BNP on extubation outcome: To determine the value of percent change in the BNP level during the 2-h. SBT that best predicts the extubation outcome; we analyzed the data from the 32 patients who passed the 2-h. SBT using the ROC curve. The area under the ROC curve was 0.96. A change of BNP level $< 20\%$ from baseline had the best combination of sensitivity [85.71%], specificity [90.91%], positive [96.77%] and negative [66.67%] predictive values and diagnostic accuracy [90%] in predicting extubation failure (Fig. 1).

Discussion

Weaning patients from mechanical ventilation continues to pose a challenge to clinicians for its complications with time [11]. A successful weaning from mechanical ventilation depends not only on adequate respiratory strength and endurance but also on optimal performance of other organs including the heart. The patient cardiovascular function may be compromised by alterations in lung volume and intrathoracic pressure during withdrawal of mechanical ventilation and may be an important cause of weaning failure [12].

Cardiovascular dysfunction is mainly associated with an increase in cardiac preload and afterload caused by intra-thoracic pressure shift and an increase in catecholamine secretion and work of breathing [13].

Diagnosing left ventricular dysfunction in patients who fail to wean is clinically difficult using the traditional methods such as echocardiography, cardiac CT scan and pulmonary artery catheterization that are either operator-dependent, lack sensitivity, not available at the bedside and invasive. The use of pulmonary artery catheter remains the gold standard to identify

Table 3 Clinical characteristics of different study groups.

Characteristics	Study groups			p -Value
	SBT Failure	Extubation Failure	Extubation Success	
Number of patients	8	7	25	
Age; mean \pm SD in years	50 \pm 9.49	54 \pm 9.25	46 \pm 10.35	0.208
Gender; Male:Female	6:2	5:2	15:10	0.686
<i>Causes of ARF (number & percentage)</i>				
ARDS	2 (16%)	2 (16%)	8 (66.6%)	0.707
COPD	1 (25%)	2(50%)	1 (25%)	0.170
Pneumonia	1 (8.33%)	1 (8.33%)	10 (83.3%)	0.268
Sepsis	5 (41.6%)	4(33.3%)	3 (25%)	0.724
<i>Comorbidity (number & percentage)</i>				
Hypertension	7 (25%)	4 (14.3%)	17 (60.7%)	0.414
Diabetes Mellitus	3 (15.8%)	5 (26.3%)	11 (57.9%)	0.359
Ischemic Heart Disease	0 (0%)	2 (25%)	6 (75%)	0.276
<i>Risk Factor (number & percentage)</i>				
Smoking	6 (25%)	5 (20.8%)	13 (54.2%)	0.407
APACHE II Score (mean \pm SD)	18 \pm 1.07	17.43 \pm 0.98	18.24 \pm 1.88	0.512
Mechanical ventilation days (mean \pm SD)	15.4 \pm 6.3	12.8 \pm 7.4	9.5 \pm 4.2	0.78

Table 4 BNP level before and after SBT in different study groups.

BNP level (pg/ml)	Study groups			<i>p</i> -Value
	SBT failure	Extubation failure	Extubation success	
Before SBT	853.1 ± 471.3	592.5 ± 271.7	543 ± 131.1	0.173
After SBT	1166.38 ± 189.7	795.29 ± 256.37	407.32 ± 202.41	0.004

Table 5 The mean percent change in plasma BNP level during 2-h. SBT.

	Study groups			<i>p</i> -Value
	SBT failure	Extubation failure	Extubation success	
Percent change [increase/decrease]	36.723% [Inc.]	34.226% [Inc.]	24.987% [dec.]	< 0.001

Table 6 correlation between BNP level before SBT& LVEF%.

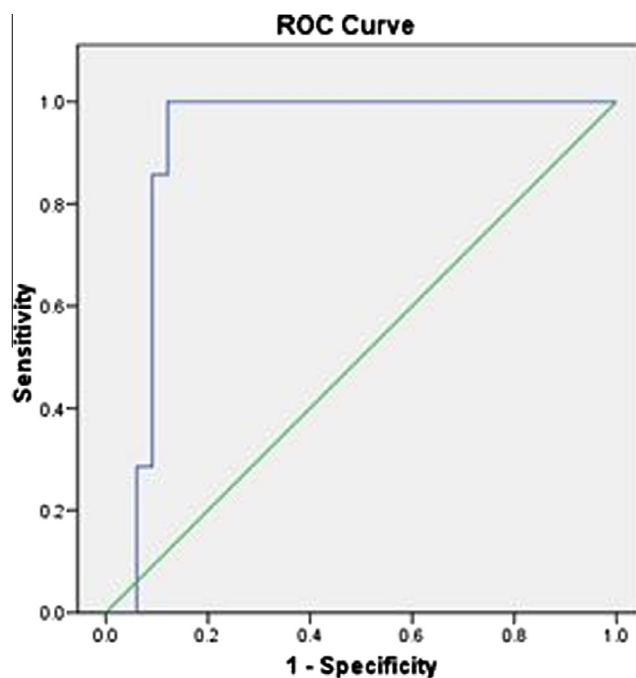
	BNP before SBT	LVEF%	<i>p</i> -Value
SBT failure	853.1 ± 471.3	58.7 ± 3.47	0.18
Extubation failure	592.5 ± 271.7	60.3 ± 5.33	0.21
Extubation success	543 ± 131.1	62.5 ± 7.9	0.14

left ventricular dysfunction during weaning [14] but measuring pulmonary artery occlusion pressure can be difficult in dyspneic patients [15]. Echocardiography may help to identify heart failure during weaning but lack of trained personnel and the needs for a good echocardiographic window limit its application [16].

The 2 h spontaneous breathing trial (SBT) is currently the most accurate index for predicting weaning success, but the extubation failure rate is still high (15–20%) in patients who have passed SBTs [1].

In patients on positive pressure ventilation, cardiovascular dysfunction may be difficult to detect [17]. During the negative pressure SBT, venous return is augmented, left ventricular trans-mural pressure and after load may also be increased [18]. These stresses placed on the heart during SBT may unmask subclinical cardiovascular dysfunction. Lemaire et al. (1988) studied 15 patients with cardiovascular disease and chronic obstructive pulmonary disease. They found that the pulmonary capillary wedge pressure was normal before SBT but increased significantly after unsuccessful SBT [5].

B-type natriuretic peptide (BNP) is a plasma neurohormone composed of 32 amino acid protein secreted by ventric-

**Figure 1** Predictive value of percent change in BNP.

ular cardiomyocytes in response to myocardial stretch [7]. Alternative sites for secretion are atria and brain. Plasma BNP levels are elevated in patients with left ventricular dysfunction [8], acute congestive heart failure [9], and right ventricular dysfunction [10]. BNP is secreted in response to

Table 7 ABG before and after SBT in different study groups.

ABG Parameter	Study Groups								
	SBT failure			Extubation failure			Extubation success		
	Before SBT	After SBT	<i>p</i> -Value	Before SBT	After SBT	<i>p</i> -value	Before SBT	After SBT	<i>p</i> -Value
PH	7.38 ± 0.04	7.35 ± 0.03	0.16	7.42 ± 0.03	7.33 ± 0.03	0.14	7.45 ± 0.05	7.45 ± 0.03	0.34
Po ₂ (mm Hg)	87.4 ± 18.6	74.6 ± 20.1	0.01	90 ± 17	78 ± 14	0.02	96 ± 25	94 ± 20	0.82
PCo ₂ (mm Hg)	37.3 ± 6.3	39.4 ± 7.5	0.60	39 ± 6	45 ± 9.2	0.41	36 ± 4.1	35 ± 4.3	0.68
Sat %	95.13 ± 2.3	87 ± 0.89	0.02	93 ± 1.8	85 ± 0.82	0.03	97.0 ± 0.82	96.8 ± 1.05	0.51

different stimuli particularly volume overloads and increased cardiac wall stretch [7]. BNP is a sensitive and specific serum marker for cardiovascular dysfunction as it is correlated to left ventricular filling pressure [8].

Two B-type natriuretic peptides are detectable in the circulation after proteolysis of a precursor molecule [proBNP]: BNP (Brain natriuretic peptide) and NT-proBNP (amino-terminal portion of proBNP). Their circulating half-life is 20 and 120 min, respectively [9]. Both are considerably high in acute and chronic heart failure [19].

Since cardiac dysfunction can cause weaning failure in patients on mechanical ventilation; we aimed in this study to investigate whether BNP level may enhance the predictive value of a 2-h. SBT for successful extubation. We hypothesized that BNP could be an alternative to pulmonary catheter or echocardiography in SBT. For this purpose we studied 40 mechanically ventilated patients recovering from respiratory failure to determine the predictive value of BNP measured during a 2-h. SBT on weaning outcome. The studied patients were recruited within the period between May 2010 and June 2011 from the critical care department; Cairo university. Patients were divided according to the result of the 2-h SBT into 3 groups: SBT failure [8 pts.], extubation success [25 pts.] and extubation failure [7 pts.].

Age and sex determine 30% of the variability in BNP levels [20]; in healthy subjects [21] and in those with heart failure [22], BNP levels increase with age. Similarly; the BNP level is 25–50% higher among women as compared with men [21]. This difference is probably because of hormonal effects [estrogen stimulates the secretion of BNP] [23]. In our study we did not find any statistically significant difference between the different studied groups as regards age and gender (p -value 0.208 & 0.686, respectively). Our results helped to nullify the age as an important factor influencing increase of BNP concentrations in ICU patients. This was in agreement with a study done by Jung et al. (2008) who studied fifty-two patients recovering from acute respiratory failure [24]. He found no significance for age and gender in both testing and validation groups (p -value 0.41, 0.07 & 0.25). Our result was contradicted by a study done by Principi et al. (2009) [25] who studied thirty patients admitted to ICU; they found that age was the only variable that showed a statistically significant difference between various studied groups especially in the heart failure group ($p < 0.05$).

Our study did not find any significant difference for the APACHE II score among the three studied groups with a p -value of 0.512 (table 3). This result coincides with the study done by Principi et al. (2009) who found no significant difference between the studied groups as regards the APACHE II, SAPS II and MODS score [25]. Similarly; Gang et al. (2013) studied 29 postoperative mechanically ventilated patients for N-terminal pro-hormone BNP and found no significant difference between the studied groups regarding age, sex, body mass index and APACHE II score ($p > 0.05$) [26].

The cause of respiratory failure in the studied groups was attributed to ARDS, COPD, pneumonia and sepsis. Although we did find any statistically significant difference between the studied groups regarding the cause (p -value 0.707, 0.170, 0.268 & 0.724 respectively); SBT and extubation failure were high among patients with sepsis. This may be related to the fact that elevation of BNP in sepsis and septic shock is correlated with the severity of cardiac dysfunction associated with sepsis [27]

and could be explained in part by the induction of cytokines such as IL-1 β and IL-6 and also by impaired neutral endopeptidase activity [28].

BNP has proved to be a powerful diagnostic [29] and prognostic marker [30] for heart failure, whether systolic, diastolic, valvular or ischemic. BNP is the most reliable hormonal marker for left ventricular dysfunction and its plasma levels correlate closely with indices of systolic function in patients with stable and decompensated heart failure [31]. In right heart disease BNP is elevated in the subgroups with pulmonary hypertension [32].

Echocardiography was done in our study 2 h. before SBT to exclude left ventricular dysfunction by estimating ejection fraction to alleviate the role of heart failure in elevation of BNP levels. Our study did not find any significant correlation between BNP and LVEF in the three studied groups. This is in concordance with the study done by Jung et al. (2008) who studied fifty-two patients recovering from acute respiratory failure to determine the predictive value of BNP; they found no significant correlation between EF% 2 h before SBT and BNP level [24].

In this study, we investigated whether BNP levels may enhance the predictive value of a 2 h. SBT for successful extubation. We found that patients who were extubated successfully have much lower BNP level after SBT than before SBT unlike both SBT and extubation failure groups who found to have higher BNP with a p -value of 0.004.

Our findings were similar to the results of Jung et al., 2008 who found that patients who were extubated successfully had much smaller plasma BNP level during 2 h. SBT than patients who failed extubation in both testing and validation group (225 vs. 305 & 394 vs. 401 pg/ml respectively) [24]. Similarly; Chien et al. (2008) found patients who required re-intubation after a previous successful SBT had a higher increase of BNP than patients who were successfully extubated (471 vs. 174 with a p -value > 0.05) [33].

Recently our results were validated by a study done by Gang et al. (2013) who evaluated the relationship between NT-pro BNP and weaning outcomes and its ability to predict weaning success in cancer patients with pulmonary complications; he found that plasma NT-proBNP was significantly higher in the weaning failure group than in the weaning success group (829 vs. 345 ng/L respectively with a p -value 0.041) [26].

Another Study by Grasso et al. (2007) evaluated the usefulness of serial Plasma NT-proBNP assays for detecting acute cardiac dysfunction during weaning failure in difficult to-wean COPD patients. Baseline NT-proBNP levels were significantly higher in patients with cardiac dysfunction and increased significantly at the end of the T-piece trial only in those patients (median 12.733, p -value < 0.05) [34].

At 2006 Mekontso-Dessap studied 102 patients during weaning from mechanical ventilation and found that BNP elevation before weaning was an independent factor for weaning failure [35]. However, despite a good prediction of SBT outcome, baseline BNP did not significantly differ between patients with successful and those failing weaning. The same was found by Chien et al. (2008) who showed no difference in the baseline BNP levels but the extubation failure group had a significantly greater increase in BNP at the end of the 2 h. T piece trial than the extubation success group with a p -value < 0.001 [33].

In our study we determined the value of percent change in the BNP level during the 2-h. SBT that best predicts the extubation outcome. We analyzed the data from the 32 patients who passed the 2-h. SBT and found that both extubation and SBT failure groups had significantly larger percent increase in BNP level, indicating inadequate cardiac reserve which might contribute to subsequent respiratory insufficiency and re-intubation unlike the extubation success group who had significantly percent decrease in BNP level with a p -value < 0.001 .

We also evaluated the percent change in the BNP level that best predicts the extubation outcome using the ROC curve. The area under the ROC curve was 0.96. It was found that change of BNP level $< 20\%$ from baseline had the best combination of sensitivity [85.71%], specificity [90.91%], positive [96.77%] and negative [66.67%] predictive values and diagnostic accuracy [90%] in predicting extubation failure.

Our findings were in agreement with a study done by Jung et al. (2008) [24] who found no difference in the baseline BNP levels, but the median percent change in the plasma BNP level during the 2-h. SBT in the extubation success group was significantly smaller than those in SBT and extubation failure groups with a p -value < 0.001 . The area under the ROC curve was 0.93 and the increase of $< 20\%$ during SBT had the best combination of sensitivity, specificity, positive and negative predictive values and diagnostic accuracy in predicting extubation success (91%, 88%, 70% & 91%).

In a study of 102 patients during weaning from mechanical ventilation by Mekontso-Dessap et al. (2006), they found that despite baseline BNP levels being associated with weaning failure and longer weaning duration, the change of BNP level during 1-h. SBT could not differentiate between patients of extubation success and extubation failure [35]. This finding contradicts ours but this can be explained by; the sampling interval for BNP in our study was longer (2 h.) than in this study which is 1 h. This emphasizes that duration of SBT may be of great importance owing to the half life time of BNP as it might not begin to increase until the patients have been on SBT for a longer period of time. A cutoff value of 275 pg/ml was specific for separating patients with successful versus failed weaning (sensitivity [83%], specificity [90%], positive [93%] and negative [79%] predictive value). Area under the curve to predict weaning failure was 0.89.

Another Study by Chien et al. (2008) [33] found no difference in the baseline BNP levels but the extubation failure group had a significantly greater increase in BNP at the end of 2-h. SBT than the extubation success group (32.7% vs. 0.69%, $p < 0.001$). An increase of BNP $< 20\%$ was validated in an independent cohort as improving the prediction of extubation success to 95% from 78% using T-piece trial.

Our results were in agreement with a study done by Lluís et al. (2011) [36] who studied 100 patients on MV for more than 48 h. who underwent a SBT. An increase of BNP showed a diagnostic and prognostic accuracy for heart failure as the cause of weaning failure of 88.9% (p -value < 0.001).

Conclusion

Measurements of BNP and its relative changes could be a useful biomarker augmenting the value of SBT in prediction of weaning outcome.

Conflict of interest

None declared.

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